

Applicants: Virginia W. Cornish
Serial No.: Not Yet Known
Filed : Herewith
Page 6

REMARKS

By this Preliminary Amendment, applicant has canceled claims 1-132 and 138-140 solely to reduce the filing fee. Accordingly, claims 133-137 and 141-157 are pending in the subject application.

Applicants point out that the subject application is a divisional application of U.S. Serial No. 09/768,479, filed January 24, 2001, which is pending on November 10, 2003, i.e. copending with the subject application. The subject divisional application has been filed to pursue the subject matter of claims 133-137 and 141-157, which subject matter was not elected in response to a September 5, 2002 restriction requirement in U.S. Serial No. 09/768,479.

Applicants also point out the subject divisional has been filed with a revised specification to account for amendments to the specification of the parent application pursuant to 37 C.F.R. 1.53(b). No new matter has been added by the revised specification.

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents which are listed on Form PTO-1449 **(Exhibit A)** and are also listed below.

This Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b)(3) before the mailing of a first Office Action on the merits. Thus, this Information Disclosure Statement should be entered and considered.

This application is a divisional application of U.S. Serial No. 09/768,479, filed January 24, 2001. Copies of the documents

Applicants: Virginia W. Cornish
Serial No.: Not Yet Known
Filed : Herewith
Page 7

listed below as items 1-48 have previously been submitted to, or cited by, the U.S. Patent Office in connection with U.S. Serial No. 09/768,479, upon which the subject application relies for an earlier filing date under 35 U.S.C. §120. Therefore, in accordance with 37 C.F.R. §1.98(d), copies of the previously submitted documents are not provided.

1. U.S. Patent No. 5,736,343 (Landry) issued April 7, 1998;
2. U.S. Patent No. 5,468,614 (Fields et al.) issued November 21, 1995;
3. U.S. Patent No. 5,314,817 (Schultz, P.) issued May 24, 1994;
4. U.S. Patent No. 5,194,594 (Kwawli et al.) issued March 16, 1993;
5. PCT International Application Publication No. WO 99/10510 (Natesan et al.) published March 4, 1999;
6. PCT International Application Publication No. WO 99/10508 (Natesan et al.) published March 4, 1999;
7. PCT International Application Publication No. WO 98/13353 (Whitney et al.) published April 2, 1998;
8. PCT International Application Publication No. WO 97/31113 (Rickles et al.) published August 28, 1997;
9. PCT International Application Publication No. WO 96/30540 (Tsien et al.) published October 3, 1999;
10. European Patent Application Publication No. EP 0 742 015

Applicants: Virginia W. Cornish
Serial No.: Not Yet Known
Filed : Herewith
Page 8

(Kadow et al.), published November 13, 1996;

11. Austin DJ, et al. Proximity versus allostery: the role of regulated protein dimerization in biology. 1994. Chem Biol. 1(3): 131-6;
12. Belshaw PJ, et al. Controlling protein association and subcellular localization with a synthetic ligand that induces heterodimerization of proteins. 1996. Proc. Natl Acad Sci USA 93(10):4604-7;
13. Belshaw PJ, et al. Controlling programmed cell death with a cyclophilin-cyclosporin-based chemical inducer of dimerization. 1996. Chem. Biol. 3:731-738;
14. Choi J, et al. Structure of the FKBP-12-Rapamycin complex interacting with the binding domain of human FRAP. 1996. Science 273(5272):239-42;
15. DeGrado WF, et al. Screening, selection and design: standing at the crossroads in three dimensions. 1997. Current Opinion in Structural Biology 7:455-456;
16. Diver SR, et al. Single-step synthesis of cell-permeable protein dimerizers that activate signal transduction and gene expression. 1997. J. Am. Chem. Soc. 119, 5106-5109;
17. Ho SN, et al. Dimeric ligands define a role for transcriptional activation domains in reinitiation. 1996. Nature. 382(6594):822-6;
18. Holsinger LJ, et al. Signal transduction in T lymphocytes using a conditional allele of Sos. 1995. Proc. Natl. Acad. Sci. USA 92:9810-9814;

Applicants: Virginia W. Cornish
Serial No.: Not Yet Known
Filed : Herewith
Page 9

19. Hung DT, et al. Understanding and controlling the cell cycle with natural products. 1996. Chem. Biol. 3:623-639;
20. Klemm JD, et al. Dimerization as a regulatory mechanism in signal transduction. 1998. Annu. Rev. Immunol. 16:569-92 ;
21. Liberles SD, et al. Inducible gene expression and protein translocation using nontoxic ligands identified by a mammalian three-hybrid screen. 1997. Proc. Natl. Acad. Sci. USA 94(15):7825-7830;
22. Licitra EJ, et al. A three-hybrid system for detecting small ligand-protein receptor interactions. 1996. Proc. Natl. Acad. Sci. USA 93:12817-12821;
23. Pedersen H, et al. A method for directed evolution and functional cloning of enzymes. 1998. Proc. Natl. Acad. Sci. USA 95:10523-10528;
24. Pruschy MN, et al. Mechanistic studies of a signaling pathway activated by the organic dimerizer FK1012. 1994. Chem. Biol. 1:163-172;
25. Schreiber SL. Chemical genetics resulting from a passion for synthetic organic chemistry. 1998. Bioorganic & Medicinal Chemistry 6:1127-1152;
26. Spencer DM , et al. Controlling signal transduction with synthetic ligands. 1993. Science 262(5136):1019-1024;
27. Spencer DM, et al. Functional analysis of Fas signaling in vivo using synthetic inducers of dimerization. 1996. Curr Biol. 6(7):839-47;

Applicants: Virginia W. Cornish
Serial No.: Not Yet Known
Filed : Herewith
Page 10

28. Spencer DM, et al. A general strategy for producing conditional alleles of Src-like tyrosine kinases. 1995. Proc. Natl. Acad. Sci. 92:9805-9809;
29. Stockwell BR, et al. TGF-beta-signaling with small molecule FKBP12 antagonists that bind myristoylated FKBP12-TGF-beta type 1 receptor fusion proteins. 1998. Chem Biol. 5(7):385-95;
30. Stockwell BR, et al. Probing the role of homomeric and heteromeric receptor interactions in TGF-beta signaling using small molecule dimerizers. 1998. Curr Biol 8(13):761-70;
31. Winkler T, et al. Confocal fluorescence coincidence analysis: An approach to ultra high-throughput screening. 1998. Proc. Natl. Acad. Sci. USA 96:1375-1378;
32. Yang J, et al. Small-molecule control of insulin and PDGF receptor signaling and the role of membrane attachment. 1997. Curr. Biol. 8:11-18;
33. Zlokarnik G, et al. Quantitation of transcription and clonal selection of single living cells with beta-lactamase as reporter. 1998, Science 279(5347):84-8;
34. Search Report dated May 14, 2001 corresponding PCT International Application No. PCT/US01/02285;
35. Amara, J. F. et al.: A versatile synthetic dimerizer for the regulation of protein-protein interactions, Proc. Natl. Acad. Sci. USA, Vol. 94, 1997, pages 10618-10623;

Applicants: Virginia W. Cornish
Serial No.: Not Yet Known
Filed : Herewith
Page 11

36. PCT International Search Report dated July 17, 2003 corresponding to PCT International Application No. PCT/US02/40943;
37. Pollock et al. Demerizer-regulated gene expression. Current Opinion in Biotechnology (2002) 13:459-467;
38. U.S. Patent No. 6,200,759, issued March 13, 2001 to Dove, S., et al.;
39. U.S. Patent No. 5,925,523, issued July 20, 1999 to Dove, S., et al.;
40. U.S. Patent No. 5,928,868, issued July 27, 1999 to Liu, H. et al.;
41. Lin, H., et al. Dexamethasone-Methotrexate: An Efficient Chemical Inducer of Protein Dimerization *In Vivo*. 2000. J.Am.Chem.Soc. 122:4247-4248;
42. Kopytek, S.J., et al. Chemically Induced Dimerization of Dihydrofolate Reductase by a Homobifunctional Dimer of Methotrexate. 2000. Chem Biol. 7:313-321;
43. Firestine, S.M., et al. Using an AraC-Based three-hybrid system to detect biocatalysts in vivo. 2000. Nature Biotechnology. 18, 544-547;
44. Pelletier, J.N., et al. Oligomerization domain-directed reassembly of active dihydrofolate reductase from rationally designed fragments. 1998. Proc.Natl.Acad.Sci.USA. 95, 12141-12146;

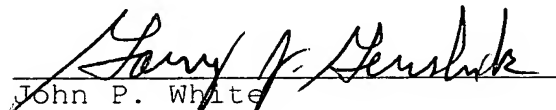
Applicants: Virginia W. Cornish
Serial No.: Not Yet Known
Filed : Herewith
Page 12

45. Ladant, D., Karimova, G. Genetic systems for analyzing protein-protein interactions in bacteria. 2000. Res. Microbiol. 151, 711-720;
46. U.S. Serial No. 10/056,874, filed January 24, 2002;
47. U.S. Serial No. 10/084,388, filed February 25, 2002; and
48. U.S. Serial No. 10/132,039, filed April 24, 2002.

Applicants request that the Examiner review the references and make them of record in the subject application.

No fee, other than the enclosed \$403.000 application filing fee, is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,


John P. White
Registration No. 28,678
Gary J. Gershik
Registration No. 39,992
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400